

Neisseria meningitidis in urogenital infection

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The routine use in this department of an immunofluorescence method in the identification of suspected colonies of gonococci has led in the past 6 months to the recognition of three cases of probable urogenital tract infection with *Neisseria meningitidis*. In each of these cases, cultures of Gram-negative diplococci were obtained which gave weaker fluorescence with antigenococcal globulin than is usually seen with gonococci and which on further investigation proved to be meningococci.

Case reports

Case 1A, an antique dealer aged 30, attended in late 1972. He had had intercourse only with his fiancée over the past year; the last time was 7 days before the consultation, and orogenital intercourse 2 days before that. For 4 days he had had a yellow urethral discharge with slight dysuria.

Examination

There was a red swollen meatus and a thick purulent yellow discharge. The urine was hazy and contained many threads. A presumptive diagnosis of gonorrhoea was made after finding intracellular Gram-negative diplococci in profusion, but in view of the history a full laboratory investigation of the organism was requested.

Treatment

The then standard treatment of gonorrhoea was given—i.e. probenecid 2 g. and ampicillin 2 g. by mouth followed by an injection of 3.6 m.u. of procaine penicillin.

Result

The signs and symptoms had disappeared by the third day and a week later all was normal. He was not seen again.

Case 1B

His fiancée attended as a suspected gonorrhoea contact. She had no symptoms and had been taking oral contraceptives (Minovlar) for a year. She had a marked cervical erosion but repeated smears and cultures were completely to reduce nonspecific fluorescence. Smears for fluorescent staining were made with normal saline, dried in air, and fixed with acetone for 10 minutes. They were

negative for all pathogens. Cervical cytology disclosed a moderate cervicitis. A week later a throat swab produced a scanty growth of an organism which was identical with that found in the male partner. A month later the gonococcal complement-fixation test was positive. The throat swabs became negative after a week's course of cotrimoxazole.

Case 2, was a passive homosexual and habitual repeater. He had been seen in July, 1970, with rectal gonorrhoea, in November, 1970, with perianal warts, and again in July and November, 1972, with further rectal gonorrhoea. He returned in March, 1973, with vague symptoms of rectal discomfort. There was evidence of proctitis and culture of a rectal swab yielded a Gram-negative diplococcus which gave only weak fluorescence with antigenococcal conjugate. No contacts were known and throat swabs before treatment with cotrimoxazole were negative.

In July, 1973, the patient was again found to have rectal gonorrhoea; *N. gonorrhoeae* was cultured from both rectum and throat. He has since had yet another attack of gonorrhoea and not surprisingly the gonococcal complement-fixation test is positive.

Case 3

A married woman started to have frequency of micturition and a yellow discharge in early May, 1973. Examination showed mild cervicitis with negative smears but cultures revealed a *Neisseria sp.* similar to those recovered from the three previous patients. She was treated with cotrimoxazole, but as she left London for an unknown address no follow-up was possible; her husband was not seen.

Material and methods

Swabs of material from the urethra, cervix, rectum, and oropharynx (including the tonsils) were inoculated on a modified Thayer-Martin medium (Riddell and Buck, 1970) and incubated in candle extinction jars at 37°C. for 48 hrs. Oropharyngeal swabs were cultured in addition on Oxoid DST agar containing 5 per cent. haemolysed horse blood.

Oxidase-positive colonies were examined by Gram stain and in films treated with antigenococcal globulin conjugated with fluorescein isothiocyanate (Difco). Before staining, the conjugate was absorbed with liver powder

then covered with a drop of the absorbed conjugate, placed in a humid chamber for 1 hour at 37°C., washed twice in phosphate buffered saline pH 7.2 for 10 min. each, blotted dry, mounted in glycerol pH 7.2, and examined under a Gillett and Sibert Conference microscope with a Turner interference filter for blue light. Colonies which gave only weak fluorescence were sub-cultured for further investigation. This comprised inoculation on serum agar slopes containing 1 per cent. glucose, maltose, fructose, lactose, and sucrose (Southern Group Laboratory), examination for growth on plain nutrient agar, culture at room temperature, and comparison of growth in pure air and in a candle jar. Cultures showing the characteristics of *N. meningitidis* were examined by slide agglutination with polyvalent and Group A, B, C, and D antimeningococcal sera (Burroughs Wellcome). Sensitivities were determined by the disc method.

For the evaluation of fluorescence of the suspected meningococcal strains, smears were prepared from these, from five strains of freshly isolated gonococci, and from type strains of *N. meningitidis*: Group A (N.C.T.C. 10025), Group B (N.C.T.C. 10026), and Group C (N.C.T.C. 8554). These were treated with doubling dilutions of the absorbed conjugate, ranging from 1 in 2 to 1 in 32, and the intensity of observed fluorescence was recorded by + signs, + to +++++ (Table).

Results

The direct microscopic examination for intra- and extracellular Gram-negative diplococci was positive only in Case 1A. Culture of his urethral discharge and the throat swab of his female partner (Case 1B) yielded an identical Gram-negative diplococcus which showed only weak fluorescence with anti-gonococcal conjugate. The organism produced acid from glucose and maltose but not fructose, lactose, and sucrose. It was catalase- and oxidase-positive and failed to grow at room temperature. Growth was enhanced by, but not dependent on, CO₂ and was reduced on plain nutrient agar. The organism was agglutinated by polyvalent and Group B anti-meningococcus serum, but not with Group A, C, and D antimeningococcus sera. It was sensitive to sulphonamide, penicillin, tetracycline, erythromycin, cephaloridine, and cotrimoxazole.

The gonococcal complement-fixation test in this patient's female contact was found to be positive on two occasions. There was no clinical or bacteriological evidence of past or present gonorrhoea in her case and it is likely that the positive complement-fixation test was a reflection of the known antigenic relationship of *N. meningitidis* and *N. gonorrhoeae* (Wilson, 1956; Danielsson, 1965).

Organisms which were morphologically and culturally identical with those described in the first patient and his female contact were isolated from the other two patients. One, from the rectum of patient 2, belonged to serogroup B, and the other, from the urethra and cervix of patient 3, to Group Y of *N. meningitidis*.

The results of titration of the conjugate with three patients' strains, five strains of freshly isolated gonococci, and three type strains of *N. meningitidis* used as controls are shown in the Table. None of the patients' cultures nor the three type cultures of *N. meningitidis* gave the 4+ fluorescence shown by the gonococcal strains. If a fluorescence of at least 2+ intensity is accepted as the minimum for a positive test, it will be seen that none of the test strains or the control strains of *N. meningitidis* gave this degree of fluorescence with conjugate diluted 1 in 2 or more. In contrast all *N. gonorrhoeae* strains showed fluorescence of at least 2+ intensity with dilutions of up to 1 in 8, and with one strain up to 1 in 16.

Discussion

The cultural and serological examination of the strains isolated from the four patients confirmed that they were *N. meningitidis*. There was no clinical evidence of a systemic infection with this organism in any of these patients. With the exception of the female contact of the first patient all others had negative oropharyngeal cultures for meningococci.

The isolation of *N. meningitidis* from the site of disease does not prove *per se* that this organism is the cause of it. There seems, however, little doubt in the case of the first patient that the intracellular Gram-

TABLE Titre of fluorescent antigonococcal globulin (FAGG) absorbed with liver powder

[illegible]

negative diplococci seen in the film of the urethral discharge, and identified by culture as meningococci, were the cause of his illness. The possibility of these organisms having been superimposed on a non-specific urethritis is unlikely in view of the prompt and lasting response of his condition to penicillin treatment.

In the other two patients it can only be surmised that the meningococci isolated from the urethra and cervix of one patient and the rectum of the other were the cause of their illness.

N. meningitidis has been known as a rare cause of infection of the male and female urogenital tract. The majority of cases reported were associated with other manifestations of disseminated meningococcal disease (Tillett and Brown, 1935; Appelbaum, 1937; Murray, 1939; Laird, 1944; Keys, Hecht, and Chow, 1971). There are, however, reports of isolations of meningococci from the urogenital tract without involvement of other organ systems. Thus Carpenter and Charles (1942) found Group A meningococci in seven patients—six male and one female—with a primary genital tract infection thought initially to be gonorrhoea. Gregory and Abramson (1971) found this organism in the vagina of a 5-year-old girl with no other symptoms than those of a vaginitis.

The isolation of *N. meningitidis* of an identical serotype from the anterior urethra of our first patient, and from the throat of his female partner with whom he had had orogenital contact, raises the question whether his infection was secondary to that of his partner. It is well known that a proportion of the normal population carry meningococci in their throat and the majority of these belong to serotype B which was found in this couple (Fraser, Bailey, Abbott, Gill, and Walker, 1973). The assumption that the urethral infection of the first patient was caused by meningococci from his partner's throat is supported by the observation of Brown, Kraus, and Arko (1973). These authors described a chimpanzee who carried *N. meningitidis* in his throat and from whose urethra, following frequent auto-orogenital contact, an identical organism was cultured on three occasions. It is possible that the transfer of *N. meningitidis* by orogenital contact from the throat of a carrier to the urethra of his or her partner is not so rare as would appear. Only further detailed investigation of any *Neisseria* sp. obtained from the urethra which does not conform strictly with the characteristics of *N. gonorrhoeae* will reveal the frequency of this occurrence. This should be coupled with increasing awareness by clinicians of the role of orogenital contact in the spread of infection.

A corollary of the ability of the meningococcus to cause, albeit rarely, a primary infection of the

urogenital tract is the rare occurrence of meningitis due to the gonococcus. It is tempting to speculate at what stage of their phylogeny these organisms acquired their predilections for different organ systems.

Summary

Neisseria meningitidis Group B was isolated from the urethral discharge of a man and the oropharynx of his female partner with whom he had had orogenital contact.

Two further strains of *N. meningitidis*, one Group B and the other Group Y, were isolated respectively from the rectum of a man with proctitis, and the urethra and cervix of a woman with cervicitis.

The significance of these findings is discussed.

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Constatation de *Neisseria meningitidis* dans une infection uro-génitale

SOMMAIRE

Neisseria meningitidis Groupe B fut isolée dans le pus urétral d'un homme et dans l'oro-pharynx de sa partenaire féminine, avec laquelle il avait eu des contacts oro-génitaux.

Deux autres souches de *N. meningitidis*, l'une du groupe B, l'autre du groupe Y, furent isolées respectivement du rectum d'un homme atteint de rectite et de l'urètre et du col d'une femme atteinte de cervicite.

On discute la signification de ces constatations.